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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,974	02/21/2002	Joseph Rubinfeld	12636-263	2253
21971	7590	01/23/2004		
WILSON SONSINI GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 943041050				
EXAMINER MCINTOSH III, TRAVISS C				
ART UNIT		PAPER NUMBER		
1623				

DATE MAILED: 01/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/081,974

Applicant(s)

RUBINFELD ET AL.

Examiner

Traviss C McIntosh

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-21,23 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21,23 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

The Examiner of the U.S. Patent application SN 10/081,974 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to the Technology Center 1600, Art Unit 1623, attn: Examiner Traviss McIntosh.

The Amendment filed October 16, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1-21 and 25 have been amended.

Claims 22, 24, and 26-53 have been canceled.

Remarks drawn to rejections of Office Action mailed June 16, 2203 include:

112 1<sup>st</sup> paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

112 2<sup>nd</sup> paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

103(a) rejection which has been maintained for reasons of record.

An action on the merits of claims 1-21, 23, and 25 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 112***

Claims 1-21, 23, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a method for treating a cancer patient comprising administering the selected active agents, however, the claim is silent as to what is actually intended to be treated. It is noted that the claim is being interpreted as a method of treating cancer in a cancer patient.

Claim 17 is indefinite wherein the claim, which depends from claim 1 is drawn to the following: a method of treating a cancer patient comprising administering a 20(S)-camptothecin for a period of time during which 5-fluorouracil is not being administered to the patient, and then administering 5-fluorouracil to the patient, wherein the period of time during which 5-fluorouracil is not being administered is at least 1 day. Claim 17 adds the further limitation that the 20(S)-camptothecin is administered between 1-90 days before or after 5-fluorouracil, and is also administered within 1 day of when 5-fluorouracil is administered. It is unclear how the 20(S)-camptothecin can be administered within 1 day of the 5-fluorouracil when claim 1 provides that the period of time during which 5-fluorouracil is not to be administered is at least 1 day.

***Claim Rejections - 35 USC § 103***

The rejection of claims 1-21, 23, and 25 under 35 U.S.C. 103(a) as being unpatentable over Rubinfeld (US Patent 6,191,119) in view of Achterrath (US Patent 6,403,569), is maintained for reasons of record.

Claim 1 is drawn to a method of treating cancer in a patient comprising administering a 20(S)-camptothecin for a period of time during which 5-fluorouracil is not being administered, then administering 5-fluorouracil (5-FU) to the patient, wherein the period of time in which the 5-FU is not being administered is at least 1 day. Claims 2-6 provide that the 20(S)-camptothecin is administered at least 1-5 days before the 5-FU, respectively. Claims 7-11 provide that the 20(S)-camptothecin is administered at least 1, 2, 3, 4, or 5 to 90 days before the 5-FU. Claims 12-16 provide that the 20(S)-camptothecin is administered at least 1, 2, 3, 4, or 5 days after the 5-FU. Claims 17-20 provide that the 20(S)-camptothecin is administered between 1, 2, 3, or 4 to 90 days before or after the 5-FU is administered, and wherein the 20(S) camptothecin is administered within 1, 2, 3, or 4 days of when the 5-FU is administered. Claims 21 and 25 provide various cancers which the patients have, and claim 23 limits the 20(S)-camptothecin to 9-nitro-20(S)-camptothecin.

Rubinfeld teaches of methods for treating cancer comprising the use of combination therapy by coadministering to the patient a 20(S)-camptothecin (including 9-nitro-20(S)-camptothecin) in combination with for example, a synergistic antimetabolite, such as 5-fluorouracil (column 2, lines 37-67). It is noted that Rubinfeld defines coadministration to mean the administration of more than one therapeutic in the course of coordinated treatment to achieve clinical outcome, such coadministration may also be coextensive, that is, occurring during overlapping periods of time (column 5, lines 54-62).

What is not taught by Rubinfeld is to specifically use 5-fluorouracil, nor to allow for at least 1 day between the administration of the 5-fluorouracil and the 20(S)-camptothecin.

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Moreover, it is noted that while Rubinfeld does not specifically acknowledge the 1 day between the administration of the active agents, they do indeed recognize the alternative as an option, wherein they state that "such coadministration *may also be*, that is, occurring during overlapping periods of time". This clearly sets forth that the coadministration may occur during overlapping periods of time, as well as during non-overlapping periods of time.

Achterrath teaches a method of treating cancer comprising administering at least one camptothecin derivative in combination with 5-fluorouracil (column 1, lines 8-15).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the methods of the prior art and obtain the methods as claimed in the instant application with the references before them. The prior art teaches the use of 20(S)-camptothecins in combination therapy with 5-fluorouracil in treating cancers. Moreover, the prior art teaches of the synergistic effects of the combination therapy (see '119, column 4, lines 64-68) and that the active agents may be administered in delayed release forms which may delay their release from about 1 hour to about 6 months (see '119, column 7, lines 36-39). Modifying the prior art methods and optimizing the time frames required between the active agents administration is seen to require nothing more than routine skill in the art, and one of ordinary skill in the art would be appraised of methods of determining the optimum time frames for that art recognized active agents to be administered.

Applicant's arguments filed October 16, 2003 have been fully considered but they are not persuasive. Applicants argue that nowhere in the references is there a teaching or suggestion to administer a 20(S)-camptothecin and 5-fluorouracil sequentially by following the regimen of claim 1. Applicants additionally argue that Achterrath teaches a camptothecin, 5-FU, and folinic

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acid in combination for treating cancer, and not the sequential treatment regimen as set forth in claim 1. However, the examiner notes that the use of the claimed active agents in combination are known in the art to provide synergistic effects in cancer therapy. One of ordinary skill in the art would be appraised of methods of determining the optimum time frame for administering the art recognized active agents to a patient for cancer therapy.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

Application/Control Number: 10/081,974

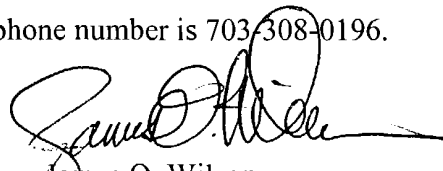
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Traviss C. McIntosh III  
January 12, 2004



James O. Wilson  
Supervisory Patent Examiner  
Art Unit 1623